

**Chemistry.** — *Formation of derivatives of dihydrobenzimidazole and tetrahydrochinoline by the action of acetic anhydride and zinc chloride on nitroderivates of alkyanilines.* By Prof. P. VAN ROMBURGH and H. W. HUYSER.

(Communicated at the meeting of June 26, 1926).

Some years ago, at this laboratory, Mr. HOEJENBOS, chem. doct<sup>s</sup>., allowed acetic anhydride and zinc chloride to react on 3.6.dinitrodiethylaniline, in order to introduce an acetylgroup, and thus to obtain an acetophenone derivative. Though this introduction did not succeed with dimethylaniline, Mr. HOEJENBOS obtained a beautifully crystalline product (mp. 127°), with the study of which, however, he could not proceed.

Some time ago we have again taken up the investigation of this substance, and at the same time have studied the action of zinc chloride on other nitro-derivates of dialkyanilines.

It was found that not only the nitro-compound, mentioned above, but also the 2.4.dinitrodiethylaniline, as well as the 3.6.- and the 2.4.dinitro-, and also the 3.4.6.trinitro-dimethylaniline gave easily crystallisable reaction products.

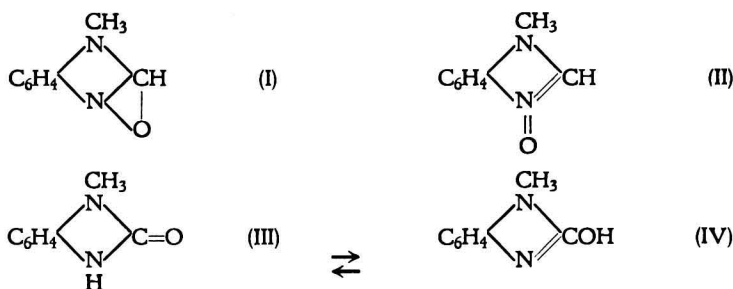
The analyses of all these compounds, which were obtained as principal products in the reaction, indicated that one acetyl group had been introduced into the molecule, and that at the same time one mol of water had been removed.

We thought at first that the acetylgroup which had been introduced, had replaced one atom of hydrogen in the benzene nucleus, but we had to give up this opinion, because a prolonged investigation proved that this acetylgroup could easily be eliminated by heating with 10% caustic potash solution, and could easily be reintroduced in some of the compounds which contained no acetyl group. The action of potash did not eliminate amines, as is the case with the unsubstituted nitro-products.

The analyses of the acetylfree compounds pointed to substances which had been formed out of the original substance by the removal of the elements of one mol of water.

The question we had to solve was: what groups from the molecule had taken part in the formation of water. It was obvious to assume that the nitro- and dialkylaminogroup, being ortho-situated, had to be considered.

The nitrated dimethylaniline derivates could then yield nitro-compounds of a substance to which might be given the following formulae:



III—IV are tautomeric compounds.

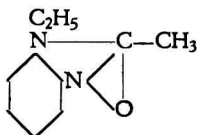
The first and the second do not contain a mobile hydrogen atom which could be replaced by acetyl. The two last, on the contrary, do. In these substances the oxygen-atom could perhaps be replaced by chlorine with simultaneous elimination of HCl, by the action of phosphorouspentachloride. This proved indeed to be the case with the anhydrocompound out of 3.6.- as well as out of 3.4. dinitrodimethylaniline.

Finally, formula III was confirmed by a synthesis. If, namely phosgene is allowed to react with 4. nitro 2. aminomethylaniline a substance is formed which is identical with the anhydro-compound formed from 2.4. dinitrodimethylaniline.

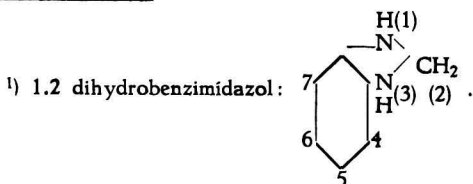
Compounds formed by the reaction of acetic anhydride and zinc chloride on the suitable nitroderivates of dimethylaniline are therefore nitroderivates of 1. methyl 2. oxo 1.2. dihydrobenzimidazol<sup>1)</sup>.

The products which are formed by the reaction of acetic anhydride and zinc chloride on nitrated diethylanilines are, as regards the results of the analyses, i.e. the empirical formulae, completely analogous with those of the methylderivates. If we assume this to be true, there are two possibilities:

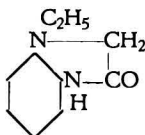
1. The hydrogen of the CH<sub>2</sub>-group of the ethylgroup can react with elimination of water, and there will appear a compound of the type



2. The hydrogen of the CH<sub>3</sub>-group of the ethylgroup can react, and



there will be formed a compound of the type

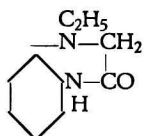


In contrast with the methylcompounds the ethyl derivatives are soluble in dilute acids, and insoluble in dilute alkalis.

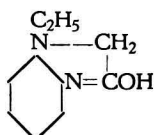
The formation of a nitroso-compound, which easily changes back into the original product by the action of strong hydrochloric acid, makes the second possibility highly probable.

Moreover, if the first formula is taken to be correct, we cannot explain why these substances so easily form an acetyl derivate, or which hydrogen-atom would be substituted in this case.

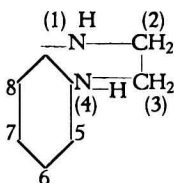
By reason of what has been said above we are justified in deriving the anhydrocompounds obtained out of the dinitrodiethylanilines from a substance with the formula :



or its tautomeric form :



They are thus derivatives of 1.2.3.4 tetrahydroquinoline :



therefore: nitrated 1 . ethyl . 3 . oxo . 1 . 2 . 3 . 4 . tetrahydroquinoxalines.

1. *The reaction of acetic anhydride and zinc chloride on some nitroderivatives of dimethylanilines.*

In the following reactions, 0.5 parts of zinc chloride and 2 parts of acetic anhydride were taken with 1 part of the substance, which, with the dinitroderivatives, was heated under a reflux condenser during 4 or 5 hours. Then the somewhat viscous reaction mixture, was diluted with a little alcohol and poured into about 40 parts of water. The separated

product was dried and boiled with benzene. The substance crystallised from the benzene solution upon cooling.

a. 3.6. dinitrodimethylaniline gives 6. nitro 1. methyl 3. aceto 2. oxo 1. 2. dihydrobenzimidazole (A), which melts at  $185^{\circ}$ — $186^{\circ}$  C.

Analysis: C 51.19, 51.02 H 4.05, 3.75 N 18.18, 18.01  
 Calculated for  $C_{10}H_9N_3O_4$  C 51.06 H 3.83 N 17.87  
 Determination of mol. weight (according to LANDSBERGER) 216, 219 calc. 235.

The substance forms almost white needles, the crystals however contain  $\frac{1}{4}$  mol of benzene (found 7.9 and 7.6, calc. 8.2).

If (A) is boiled with caustic alkali the acetylgroup is replaced by hydrogen, and a substance is formed which melts at about  $272^{\circ}$  C., slightly brown, long needles (out of alcohol), which crumble into shorter crystals after a few days.

This substance is an anhydrocompound from the original product, namely 6. nitro 1. methyl 2. oxo 1. 2. dihydrobenzimidazole (B).

Analysis: C 49.53, 49.83 H 3.73, 3.79 N 21.93, 21.72  
 Calc. for  $C_8H_7N_3O_3$  C 49.74 H 3.63 N 21.76

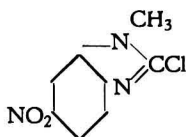
(B) was also formed when we tried to oxidize (A) with  $CrO_3$  in acetic acid solution.

The substance is soluble in caustic potash; with strong caustic potash a potassium compound is precipitated.

Treatment of (A) with iron in concentrated hydrochloric acid reduces the nitro-group, with elimination of the acetylgroup: 6. amino 1. methyl 2. oxo 1. 2. dihydrobenzimidazole (C) is formed, which crystallizes as a hydrochloride with one mol of  $H_2O$ .

Analysis: C 44.20, 44.22 H 5.77, 5.75 N 19.30, 19.23  
 Cl 16.42 16.47  
 Calc. for  $C_8H_9N_3 \cdot 0.5HCl + H_2O$  C 44.14 H 5.52 N 19.31 Cl 16.32  
 The determination of water gave 8.21 calc. 8.28.

By the reaction of phosphorouspentachloride on the anhydrocompound (B) dissolved in phosphorousoxychloride we get:



that is: 6. nitro 1. methyl 2. chlorobenzimidazole.

Analysis: N 19.65, 19.62 Cl 17.0  
 Calc. for  $C_8H_6N_3O_2Cl$  N 19.86 Cl 16.8

b. 2.4. dinitrodimethylaniline gives a compound (mp.  $175^{\circ}$ — $176^{\circ}$  C.) when treated with acetic anhydride and zinc chloride.

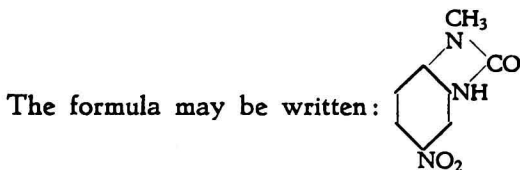
Analysis: C 51.17, 51.33 H 3.92, 3.99 N 18.00, 17.86  
 Calc. for  $C_{10}H_9N_3O_4$  (e.g.  $NO_2C_6H_3[NCH_3 \cdot CO \cdot NCOCH_3]$ ) C 51.06 H 3.83 N 17.87

This compound is the 5 . nitro 1 . methyl 3 . aceto 2 . oxo 1 . 2 . dihydrobenzimidazole (D).

Like the analogous 6 . nitro derivative this substance changes into the acetylfree anhydrocompound by heating with diluted caustic soda . mp . 300°.

Determination of nitrogen 21.86 and 21.87 N

Calc. for  $C_8H_7N_3O_3$  21.76 N.



So it is 5 . nitro 1 . methyl 2 . oxo 1 . 2 . dihydrobenzimidazole (E).

By reduction with iron and hydrochloric acid (E) passes into the aminocompound analogous to (C), which crystallised as a hydrochloride with 1 mol of  $H_2O$  (mp . 320°—330° C. under decomposition).

Determination of chlorine: Cl 16.54 and 16.47

Calc. for  $C_8H_9N_3O \cdot HCl + H_2O$  Cl 16.29.

By treating (E) with phosphorouspentachloride in a solution of phosphorousoxychloride colourless needles are formed of 5 . nitromethyl 2 . chlorobenzimidazole.

Analysis: Cl 16.90, 16.91 N 19.70, 19.53

Calc. for  $C_8H_6N_3O_2Cl$  Cl 16.78 N 19.86

By the reaction of phosgene on 4 . nitro 2 . aminomonomethylaniline, dissolved in benzene, we succeeded in synthesizing (L). The substance obtained had the same mp. as (E) and did not lower the mp. when mixed with it.

By boiling the compound (E) with glacial acetic acid we obtained the compound (D), mp. 175° C.

c. 3 . 4 . 6 . trinitrodimethylaniline also reacts with acetic anhydride and zinc chloride, but much slower. Instead of from 4 to 5 hours it is necessary to heat for 72 hours. The melting point of the reaction product obtained, which dissolves in alkali, and is then precipitated again by acids, is 294° C. It does not contain an acetylgroup, but according to the analysis, has the anhydrogroup of the original substance: therefore 5 . 6 . dinitro 1 . methyl 3 . oxo 1 . 2 . dihydrobenzimidazole (F).

Analysis: C 40.36, 40.41 H 2.55, 2.89 N 23.69, 23.64

Calc. for  $C_8H_6N_4O_5$  C 40.33 H 2.52 N 23.53.

An acetylcompound of this substance is formed when (A) is nitrated with cold nitric acid. The mp. of the substance obtained, 5 . 6 . dinitro 1 . methyl 3 . aceto 2 . oxo 1 . 2 . dihydrobenzimidazole (G) lies at about 191° C.

Analysis: C 42.70, 42.78 H 3.06, 2.88 N 20.08, 20.20

Calc. for  $C_9H_8N_4O_6$  C 42.85 H 2.85 N 20.0.

By the reaction of caustic potash, the acetylgroup is substituted by hydrogen, and a product is obtained which has the same mp. and is identical with (F).

2. *The reaction of acetic anhydride and zinc chloride on dinitrodiethylanilines.*

a. Out of 3.6. dinitrodiethylaniline is formed a substance which crystallizes in almost white needles, and which melts at 127°.

Analysis: C 54.50, 54.55 H 5.20, 5.03 N 16.18, 16.24  
 Calc. for  $C_{12}H_{13}N_3O_4$  C 54.75 H 4.94 N 15.97  
 Mol. weight (according to LANDSBERGER) Found 230 and 252, calc. 247.

This substance is 7. nitro 1. ethyl 4. aceto 3. oxo 1. 2. 3. 4., tetrahydroquinoxaline (H).

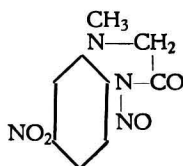
By treating (H) with a 10% aqueous solution of alkali, the acetylgroup is replaced by hydrogen, and we get again the anhydrocompound of the original substance which melts at 206° C.

Determination of nitrogen. Found 19.08 and 18.96 calc. for  $C_{10}H_{11}N_3O_3$ : 19.0 N.

This substance is 7. nitro 1. ethyl 3. oxo 1. 2. 3. 4. tetrahydroquinoxaline. (I).

By treating with sodium nitrite in a solution of dilute sulphuric acid we get a nitroso compound, which easily passes into the anhydrocompound again upon the addition of warm hydrochloric acid.

It is highly probable therefore that the nitroso-compound has the following structure:



b. According to the well known reaction we obtain out of 2.4. dinitrodiethylaniline a compound which melts at 157° C.

Analysis: C 54.21, 54.30 H 5.18, 5.35 N 19.06, 19.05  
 Calc. for  $C_{10}H_{11}N_3O_3$ , that is the original product, less 1 mol. of  $H_2O$  C 54.30 H 4.98 N 19.0.

This substance will therefore be 6. nitro 1. ethyl 3. oxo 1. 2. 3. 4. tetrahydroquinoxaline. In this case no acetyl derivative was obtained.

The synthesis of these quinoxaline derivatives is still under investigation, and in the *Recueil des Travaux Chimiques des Pays-Bas* we hope to enlarge upon the results mentioned in this paper.

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